IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	:	
Ulrich Klar et al.	:	Examiner: Celia C. Chang
Serial No.: 09/485,292	:	Group Art Unit: 1625
Filed: May 3, 2000	:	Allowed: January 23, 2008

For: EPOTHILONE DERIVATIVES, METHOD FOR PRODUCING SAME AND THEIR PHARMACEUTICAL USE

Substitute Specification Page Submission

Commissioner for Patents
P.O. Box 1450
Alexandria VA 22313-1450

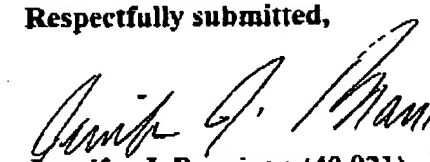
Sir:

In response to the Examiner's telephone call of 6 March 2008, requesting substitute specification pages 44-47, copies are attached.

Original specification pages 45-47 contained German text embedded in two reaction schemes followed by keys containing the English language translation of said German text. The German text has been redacted and replaced with the English translated text from the keys. The keys have been deleted. References to Figure 1 and Figure 2 have been replaced with Scheme 1 and Scheme 2.

No new matter has been added.

Respectfully submitted,



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SCH-1742

Protective groups PG that can be considered include all radicals that are known to one skilled in the art as such protective groups. Preference is given in this case to silyl-containing protective groups, such as, for example the trimethylsilyl, triethylsilyl, tert-butyldimethylsilyl, tert-butyldiphenylsilyl, tribenzylsilyl, and triisopropylsilyl radicals.

A summary of protective groups is given in, e.g., "Protective Groups in Organic Synthesis" by Theodora W. Green, John Wiley and Sons).

Halogen means fluorine, chlorine, bromine, and iodine.

The compounds of general formula II that are required for the process according to the invention can be obtained by acetylation of (4R,5S)- or (4S,5R)-4-methyl-5-phenyl-2-oxazolidinone with bromine or chlorine acetyl chloride in the presence of a strong base, such as, for example n-butyllithium.

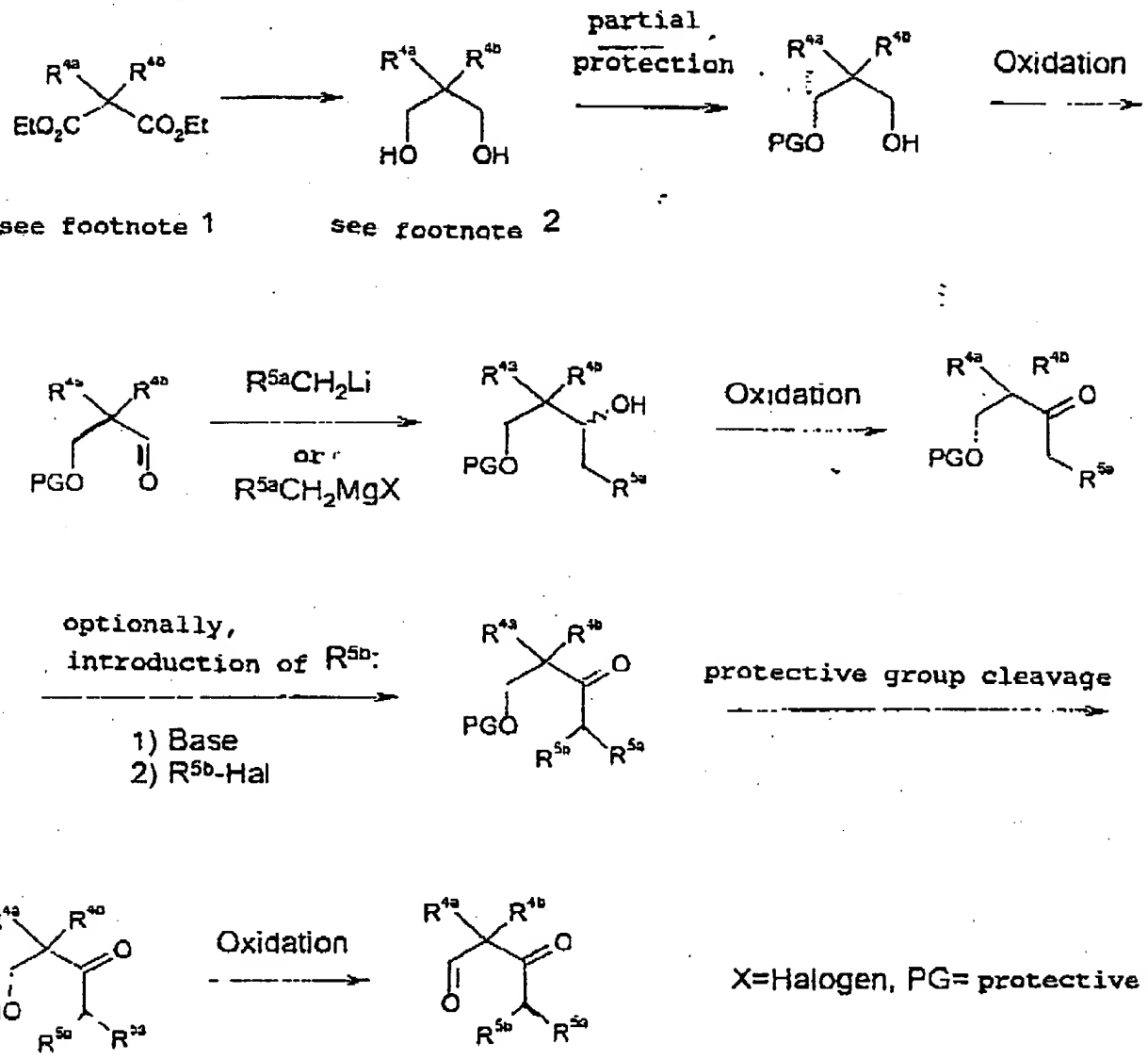
The stereochemistry of the hydroxy group in position 3 is controlled later by the selection of the chiral auxiliary.

The compounds of general formula III that are required for the process according to the invention can be obtained commercially or can easily be manufactured.

To the extent that the compounds of general formula III are not available commercially, they can be manufactured using, for example, the methods that are indicated in Schemes 1 and 2.

Scheme 1

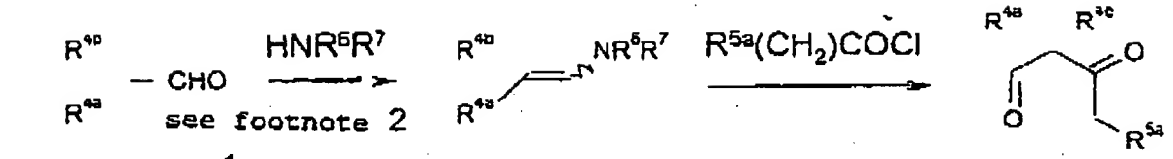
The starting material is (substituted) malonic ester.



1) In this regard see starting product C, in which $R^{4a}+R^{4b}$ = trimethylene

2) These 1,3-propanediols are available commercially to some extent and can then be incorporated into the synthesis at this point.

Scheme 2



see footnote 1

optionally, introduction of R^{5b}

1) These starting compounds are available commercially or can be obtained according to the methods that are known to one skilled in the art.

2) Secondary amine: preferably piperidine or morpholine or R^6 and R^7 mean, independently of one another, a straight-chain or branched C_1-C_6 alkyl group.